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SARCOPENIC-OBESITY AND CARDIOVASCULAR DISEASE RISK IN THE ELDERLY

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Abstract: *Objectives:* To determine: 1) whether sarcopenic-obesity is a stronger predictor of cardiovascular disease (CVD) than either sarcopenia or obesity alone in the elderly, and 2) whether muscle mass or muscular strength is a stronger marker of CVD risk. *Design:* Prospective cohort study. *Participants:* Participants included 3366 community-dwelling older (65 years) men and women who were free of CVD at baseline. *Measurements:* Waist circumference (WC), bioimpedance analysis, and grip strength were used to measure abdominal obesity, whole-body muscle mass, and muscular strength, respectively. Subjects were classified as normal, sarcopenic, obese, or sarcopenic-obese based on measures of WC and either muscle mass or strength. Participants were followed for 8 years for CVD development and proportional hazard regression models were used to compare risk estimates for CVD in the four groups after adjusting for age, sex, race, income, smoking, alcohol, and cognitive status. *Results:* Compared with the normal group, CVD risk was not significantly elevated within the obese, sarcopenic, or sarcopenic-obese groups as determined by WC and muscle mass. When determined by WC and muscle strength, CVD risk was not significantly increased in the sarcopenic or obese groups, but was increased by 23% (95% confidence interval: 0.99-1.54, P=0.06) within the sarcopenic-obese group. *Conclusion:* Sarcopenia and obesity alone were not sufficient to increase CVD risk. Sarcopenic-obesity, based on muscle strength but not muscle mass, was modestly associated with increased CVD risk. These findings imply that strength may be more important than muscle mass for CVD protection in old age.

Key words: Waist circumference, skeletal muscle, aged, longitudinal study.

Introduction

Sarcopenic-obesity represents a reduced skeletal muscle mass coupled with increased adiposity within the same elderly person (1). The limited research on the health consequences of sarcopenic-obesity has focused on functional outcomes. Some (1, 2) but not all (3, 4) studies indicate that sarcopenic-obesity, but not obesity or sarcopenia alone, is a risk factor for functional impairment.

Within the elderly, obesity, particularly abdominal and visceral obesity, contributes to numerous cardiometabolic health problems such as insulin resistance (5), type 2 diabetes (6), dyslipidemia (7), and cardiovascular disease (CVD) (7, 8). Likewise, low muscle mass and strength are associated with CVD risk factors including arterial stiffness (9), glucose intolerance (10), and the metabolic syndrome (11). As both obesity and low muscle mass/strength predict cardiovascular risk in the elderly, it is possible that the combination of obesity and sarcopenia would be associated with an even greater risk.

In support of the aforementioned notion, cross-sectional research in a sample of 871 sarcopenic-obese elderly demonstrated that abdominal obesity and low muscular strength are characterized by high circulating levels of proinflammatory cytokines (12), which are recognized risk factors for CVD (13). Conversely, in a cross-sectional study of 22 obese postmenopausal women, the CVD risk factor profile was more favorable in sarcopenic-obese women than in obese women with a normal muscle mass (14). The discrepant findings in these studies may reflect the different approaches for assessing sarcopenia (muscle strength vs. muscle mass), raising the question as to whether muscle mass or strength is more important for cardiovascular health. While these two studies provide some interesting findings, their small sample sizes, cross-sectional designs, and contradictory findings indicate that more research is needed to clarify the impact of sarcopenic-obesity on CVD risk.

The primary purpose of this study was to determine if sarcopenic-obesity was a stronger predictor of CVD risk in the elderly than either sarcopenia or obesity alone. A secondary objective was to determine whether low muscle mass or low muscular strength was a stronger marker of CVD risk.

Methods

Study Sample

The study sample included elderly men and women from the Cardiovascular Health Study (CHS), a population-based longitudinal study of CVD in older adults, as described in detail elsewhere (15). Briefly, subjects were sampled from Medicare eligibility lists in Washington County, MD; Sacramento County, CA; Forsyth County, NC; and Pittsburgh, PA. Eligible participants were 65 years and older, noninstitutionalized, able to give informed consent, and did not require a proxy respondent. Of those eligible, 5201 (57%) enrolled. The institutional review boards approved the project at each study site and written informed consent was obtained from all subjects.

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The baseline examination was conducted between June 1989 and June 1990, and the CHS cohort was followed annually for 10 years. The baseline and follow-up examinations consisted of a home or telephone interview and clinical examination (15). Briefly, in the home/telephone interview, information was obtained on demographics and medical history. The clinical examination included anthropometric measurements and a standardized clinical examination. A total of 76 individuals were excluded from the study sample because they did not grant permission to have their data included in the public access data set, 1241 were excluded due to prevalent CVD at baseline, and an additional 518 were excluded because of missing data on the study variables. Therefore, this study was limited to 3366 participants.

The CHS was conducted and supported by the National Heart, Lung, and Blood Institute in collaboration with the CHS investigators. These investigators created public access data sets that are stripped of all personal identifiers and are available, on appropriate terms and conditions, to qualified investigators. This manuscript is based on the public access data files.

Body Composition

Abdominal Obesity

Measures of abdominal obesity, as determined by waist circumference (WC), were chosen over measures of total adiposity (e.g., BMI, percent fat) as the obesity indicator given that abdominal adiposity is a stronger predictor of cardiovascular risk factors and disease (7, 8). WC was measured at baseline to the nearest 0.5 cm at the level of the umbilicus. Waist circumference is highly correlated to total (R^2 =0.68 in men, 0.87 in women), abdominal (R^2 =0.68 in men, 0.73 in women), and visceral (R^2 =0.55 in men, 0.76 in women) fat as determined by magnetic resonance imaging (16).

Sarcopenia

Sarcopenia was classified using two different approaches based on either skeletal muscle mass or skeletal muscle strength. Whole-body skeletal muscle mass was estimated using bioelectrical impedance analysis (BIA). BIA resistance was obtained using a TVI-10 Body Composition Analyzer (Danninger Medical, Columbus, OH) (15) with measurements taken between the right wrist and ankle with the subject in a supine position after completion of an overnight fast (17). Skeletal muscle mass was calculated using the equation developed by Janssen and colleagues (18): Skeletal muscle mass (kg) = [Height^2/R x 0.401) + (sex x 3.825) + (age x -0.071)] + 5.102, where height is in cm; R is BIA resistance in ohms; for sex, women=0 and men=1; and age is in years. The r^2 and standard error of this regression equation are 0.86 and 2.7 kg (9%), respectively, when compared to whole-body measures obtained by magnetic resonance imaging. Muscle mass was adjusted for height using a regression-based residual technique and is presented as such throughout the manuscript. As a measure of muscular strength, maximal dominant hand grip strength was measured 3 times using a Jamar dynamometer (Asimow Engineering Co., Los Angeles, CA) and averaged to the nearest kg (15). Grip strength was also adjusted for height using regression-based residual scores. Grip strength is a commonly employed measure of muscular strength in epidemiological studies and is well correlated with other maximal isometric strength measures using a strain-gauge system, including elbow flexion (r=0.64), knee extension (r=0.52), trunk flexion (r=0.43), and trunk extension (r=0.52) (19).

Determination of Obesity and Sarcopenia Categories

Initially, subjects were divided into sex-specific tertiles (low, moderate, and high) based on their: 1) WC, and 2) muscle mass. Subjects in the low or moderate WC tertiles and the moderate or high muscle mass tertiles were classified as having a 'normal' body composition. Subjects in the high WC tertile and either the moderate or high muscle mass tertiles were considered 'obese'. Subjects in the low muscle mass tertile and either the low or moderate WC tertile were considered 'sarcopenic'. Finally, subjects in the high WC tertile and low muscle mass tertile were classified as 'sarcopenic-obese'. A comparable classification approach to that described above (obesity X muscle mass) was used to classify subjects into four groups based on tertiles of WC and skeletal muscle strength (obesity X muscle strength).

Cardiovascular Disease

The study outcomes consisted of incident: 1) coronary heart disease (CHD) (first occurrence of myocardial infarction, silent myocardial infarction, angioplasty, or coronary artery bypass) (20), 2) congestive heart failure (CHF), 3) stroke, and 4) overall CVD (first occurrence of CHD, CHF, or stroke). Incident CVD events were ascertained over 8 years by self-report and from the Health Care Financing Administration hospitalized patient database of International Classification of Diseases, Ninth Revision diagnostic codes and are reported to the exact day (21). Confirmation of CVD-related deaths was conducted through reviews of obituaries, medical records, death certificates, and the U.S. Health Care Financing Administration healthcare utilization database for stays in hospital.

Covariates

Sex. Male or female.

Age. Age was subdivided into 4 subgroups (65-70 years, 71-76 years, 77-82 years, 83 years).

Race. White or other race.

Income. Self-reported family income was used as a proxy for socioeconomic status. Annual income was categorized as very low ($7,999), low ($8,000-$15,999), moderate ($16,000-$34,999), high ($35,000-$49,999), or very high ($50,000). Participants who did not report their income (6.3%) were coded in a separate non-response category.

Smoking. Lifetime smoking was categorized as none, passive (lived with regular smoker), light (1-13 pack-years), moderate (14-50 pack-years), or heavy (>50 pack-years) (15).

Alcohol. Weekly alcohol consumption was categorized as low (<1 drink•week^{-1}), moderate (1–7 drinks•week^{-1}), or heavy (>7 drinks•week^{-1}).

Cognitive Function. Cognitive function was measured using the 30-point Mini-Mental State Examination (22). Subjects were categorized as having normal (>24 points) or impaired (23 points) cognitive function.

Physical Activity. Participants reported their participation in the following activities over the previous 2 weeks: walking, hiking, jogging, biking, exercise cycling, dancing, aerobics, bowling, golfing, calisthenics, and swimming, plus up to two additional leisure time activities not included in this list. A weekly energy expenditure value was calculated for each subject (kcal•week^{-1}) as previously described (23), and subjects were divided into sex-specific quartiles.

Cardiovascular Risk Markers. Diabetes status was coded as present or absent based on the American Diabetes Association criteria (24). Blood pressure was coded as normal (<120/80 mmHg), pre-hypertensive (120/80–139/89 mmHg), or hypertensive (140/90 mmHg and/or medication use) (25). Total cholesterol was considered desirable (<200 mg/dL), borderline high (200–239 mg/dL), or high (240 mg/dL). HDL-cholesterol was categorized as low (<40 mg/dL), moderate (40-59 mg/dL), or high (60 mg/dL). Triglycerides were coded as normal (<150 mg/dL), borderline high (150-199 mg/dL), high (200-499 mg/dL), or very high (500 mg/dL) (26).

Statistical Analyses

SAS software version 9.1 (SAS Institute, Cary, NC) was used for data analyses. Initially, differences in the descriptive characteristics between groups were determined using general linear models with Bonferroni post-hoc tests. Because 6 pair-wise comparisons were necessary to compare all four groups to each other, a P-value of <0.008 denoted statistical significance (e.g., 0.05 / 6 = 0.008). Next age and sex-adjusted partial correlations for the anthropometric and strength measures were calculated. Finally, the risk of developing the different CVD outcomes was compared using Cox proportional hazards regression models. The normal body composition group served as the referent group in the Cox models and covariates consisted of age, sex, race, income, smoking, alcohol, and cognitive function (Model 1). To determine if physical activity and cardiovascular risk markers mediated the relationship between sarcopenic-obesity and CVD, two mediation models were created. Physical activity was included in addition to the aforementioned covariates in the first mediation model (model 2), with the CVD risk markers added to the second mediation model (model 3). Sex X group and age X group interaction terms were explored in the regression models, and without exception these were non-significant (P>0.1).

Determination of Follow-up Length for Cox Models

Participants were followed for 8 years after their baseline examination. For those who experienced a CVD event, follow-up length was the number of days between their baseline exam and the initial event. For those subjects who did not develop CVD but died during the follow-up period, the length of time between their baseline examination and death was used as their follow-up length.

Results

Subject Characteristics

Descriptive information for the 3366 subjects is shown in Table 1. When the sample was divided into the four groups using WC and SM (obesity X muscle mass), 38.7% of subjects were classified as having a normal body composition, 27.5% were sarcopenic, 28.0% were obese, and 5.8% were sarcopenic-obese (Table 2). The corresponding numbers in the groups classified according to obesity X muscle strength were 44.0%, 22.3%, 22.6%, and 11.1%. Using two different classification systems for the body composition measures resulted in some subjects switching exposure group. Of those subjects who were classified as normal based on obesity X muscle mass, 71.0% were also classified as normal based on obesity X muscle strength; the remaining 29.0% were classified as sarcopenic. Only 40.1% of the subjects who were sarcopenic based on obesity X muscle mass were also sarcopenic based on obesity X muscle strength; the remaining 59.9% were classified as normal. The majority (70.5%) of subjects who were obese based on obesity X muscle mass were also obese based on obesity X muscle strength; the remaining 29.5% were sarcopenic-obese. Finally, of those who were sarcopenic-obese based on obesity X muscle mass, 49.0% were sarcopenic-obese and 51.0% were obese based on obesity X muscle strength.

Table 1
Characteristics of study participants at baseline

Covariate	Prevalence (%)
Male	39.6
White race	94.9
Age	
65–70 years	45.8
71–76 years	32.2
77–82 years	16.3
83 years	5.6
Annual household income	
$7,999	10.2
$8,000–15,999	25.2
$16,000–34,999	34.6
$35,000–49,999	10.0
$50,000	13.9
Not Reported	6.2
Smoking status	
None	45.6
Passive (lived with regular smoker)	4.1
Light (1–13 pack-years)	13.0
Moderate (14–50 pack-years)	25.9
Heavy (>50 pack-years)	11.4
Alcohol consumption	
<1 drinks•week^{-1}	67.4
1–7 drinks•week^{-1}	19.4
>7 drinks•week^{-1}	13.3
Impaired cognitive function	4.8

Table 2
Baseline characteristics of groups according to sarcopenia and obesity classification

Variable	Normal	Sarcopenic	Obese	Sarcopenic-Obese
Obesity X Muscle Mass				
n (%)	1304 (38.7)	927 (27.5)	941 (28.0)	194 (5.8)
BMI (kg•m-²)	25.5 ± 2.6[b,c,d]	23.1 ± 2.3[a,c,d]	30.7 ± 3.4[a,b,d]	27.1 ± 2.4[a,b,c]
WC (cm)	88.0 ± 7.8[b,c,d]	85.2 ± 8.1[a,c,d]	106.1 ± 6.0[a,b,d]	103.8 ± 4.8[a,b,c]
Muscle mass (kg)	22.5 ± 6.3[b,c,d]	18.9 ± 5.4[a,c]	23.9 ± 6.5[a,b,d]	19.9 ± 5.3[a,c]
Hand grip strength (kg)	28.8 ± 10.6[b]	26.9 ± 9.87[a,c]	28.9 ± 10.4[b]	26.9 ± 10.7
Obesity X Muscle Strength				
n (%)	1481 (44.0)	750 (22.3)	762 (22.6)	373 (11.1)
BMI (kg•m-²)	24.7 ± 2.7[b,c,d]	24.0 ± 2.7[a,c,d]	30.3 ± 3.5[a,b,d]	29.6 ± 3.6[a,b,c]
WC (cm)	86.7 ± 8.0[c,d]	87.1 ± 8.2[c,d]	105.5 ± 5.8[a,b]	106.0 ± 6.1[a,b]
Muscle mass (kg)	21.2 ± 6.1[c,d]	20.6 ± 6.5[c,d]	23.6 ± 6.5[a,b]	22.7 ± 6.5[a,b]
Hand grip strength (kg)	31.5 ± 9.8[b,d]	21.2 ± 7.6[a,c]	31.9 ± 9.9[b,d]	21.7 ± 8.0[a,c]

Values are mean ± standard deviation; Significantly different from a. normal; b. sarcopenic; c. obese; d. sarcopenic-obese group (P<0.008); WC, waist circumference; BMI, body mass index.

Baseline body composition and strength details for the obesity X muscle mass groups are outlined in Table 2. BMI, WC, and muscle mass values were lowest in the sarcopenic groups and highest in the obese groups. This pattern persisted for grip strength, although the differences in the mean grip strength values of the four groups were <7%. Table 2 also contains the baseline body composition and strength details for the obesity X muscle strength groups. BMI, and grip strength values were lowest in the sarcopenic and highest in the obese subjects and despite their low grip strength, the sarcopenic-obese subjects had a higher muscle mass than subjects in the normal group.

Relation Between Anthropometric and Strength Measures

Based on partial correlations adjusted for age and sex, WC was modestly associated with muscle mass (r=0.39, P<0.0001) but was not related to grip strength (r=0.00, P>0.8). Grip strength was weakly correlated with muscle mass (r=0.13, P<0.0001). Within each of the different body composition groups the correlation coefficients between WC, muscle mass, and grip strength measures were of a similar order of magnitude (data not shown).

Cardiovascular Disease Risk

Inspection of Figure 1 reveals that, irrespective of how sarcopenic-obesity status was classified, the crude event rates for CVD were slightly higher in the sarcopenic and obese groups relative to the normal group, with the sarcopenic-obese group displaying the highest CVD event rates. Compared with the normal group, CVD event rates in the sarcopenic-obese group were elevated by 23% when based on obesity X muscle mass and 33% when based on obesity X muscle strength (Figure 1).

Table 3 presents the risk estimates for the various CVD outcomes based on the four obesity X muscle mass body composition groups. After adjustment for the basic covariates (Model 1), the risks of CVD, CHD, CHF, and stroke were not significantly elevated within the obese, sarcopenic, or sarcopenic-obese groups compared with the normal group (P>0.10).

Figure 1
Number of cardiovascular disease events per 10,000 person-years according to abdominal obesity and sarcopenia classified using either obesity X muscle mass (Panel A) or obesity X muscle strength (Panel B)

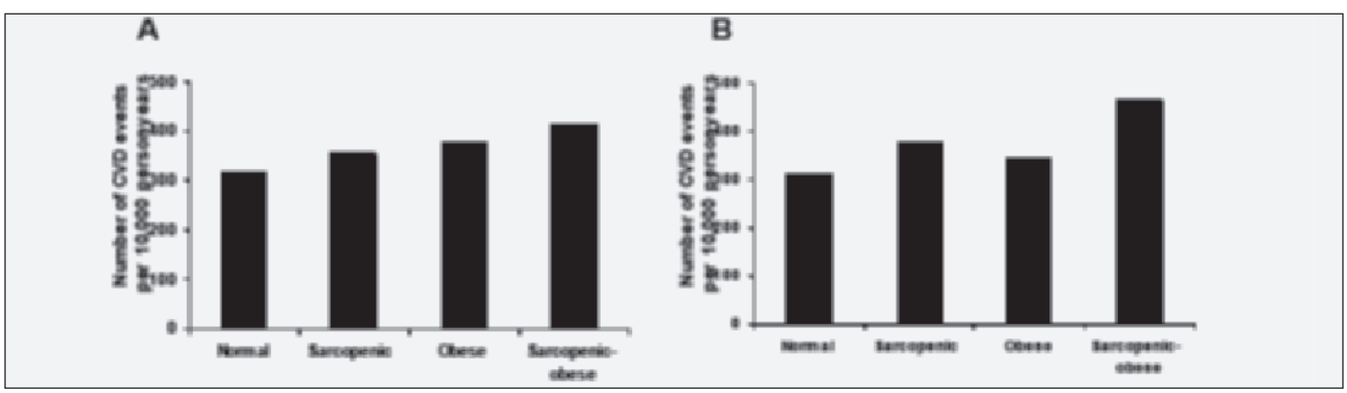

Table 3
Cardiovascular disease risk according to Obesity x Muscle Mass

	Model 1	Model 2	Model 3
Cardiovascular Disease			
Normal	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Obese	1.00 (0.84 – 1.20)	0.99 (0.83 – 1.19)	1.03 (0.86 – 1.24)
Sarcopenic	1.14 (0.96 – 1.36)	1.11 (0.93 – 1.34)	0.97 (0.81 – 1.16)
Sarcopenic-obese	1.10 (0.81 – 1.48)	1.04 (0.77 – 1.41)	0.97 (0.72 – 1.31)
Coronary Heart Disease			
Normal	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Obese	1.05 (0.82 – 1.35)	1.04 (0.81 – 1.34)	1.09 (0.84 – 1.40)
Sarcopenic	1.22 (0.96 – 1.56)	1.20 (0.94 – 1.53)	1.02 (0.79 – 1.31)
Sarcopenic-obese	0.88 (0.56 – 1.40)	0.85 (0.54 – 1.36)	0.79 (0.50 – 1.26)
Congestive Heart Failure			
Normal	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Obese	0.90 (0.69 – 1.18)	0.89 (0.68 – 1.16)	0.91 (0.69 – 1.19)
Sarcopenic	1.10 (0.85 – 1.43)	1.06 (0.82 – 1.38)	0.97 (0.74 – 1.27)
Sarcopenic-obese	1.22 (0.81 – 1.84)	1.14 (0.75 – 1.72)	1.10 (0.73 – 1.67)
Stroke			
Normal	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Obese	1.13 (0.84 – 1.51)	1.12 (0.84 – 1.51)	1.18 (0.88 – 1.59)
Sarcopenic	1.21 (0.90 – 1.61)	1.17 (0.88 – 1.57)	0.98 (0.73 – 1.32)
Sarcopenic-obese	0.97 (0.57 – 1.63)	0.92 (0.54 – 1.55)	0.79 (0.47 – 1.34)

Results are reported as hazard ratio (95% confidence interval); Model 1: adjusted for age, sex, race, income, smoking, alcohol, and cognitive function; Model 2: same as Model 1 + physical activity; Model 3: same as Model 2 + cardiovascular risk markers (diabetes, hypertension, HDL-cholesterol, total cholesterol, and triglycerides).

Table 4
Cardiovascular disease risk according to Obesity x Muscle Strength

	Model 1	Model 2	Model 3
Cardiovascular Disease			
Normal	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Obese	1.04 (0.86 – 1.25)	1.03 (0.85 – 1.24)	1.08 (0.90 – 1.30)
Sarcopenic	1.10 (0.92 – 1.33)	1.08 (0.89 – 1.30)	0.94 (0.78 – 1.14)
Sarcopenic-obese	1.23 (0.99 – 1.54)	1.18 (0.95 – 1.48)	1.06 (0.85 – 1.33)
Coronary Heart Disease			
Normal	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Obese	1.08 (0.83 – 1.40)	1.06 (0.82 – 1.38)	1.13 (0.86 – 1.47)
Sarcopenic	1.10 (0.85 – 1.42)	1.08 (0.84 – 1.39)	0.92 (0.71 – 1.19)
Sarcopenic-obese	1.29 (0.95 – 1.76)	1.25 (0.92 – 1.71)	1.11 (0.81 – 1.52)
Congestive Heart Failure			
Normal	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Obese	0.87 (0.65 – 1.15)	0.87 (0.66 – 1.15)	0.92 (0.70 – 1.22)
Sarcopenic	0.95 (0.72 – 1.26)	0.93 (0.70 – 1.23)	0.86 (0.64 – 1.15)
Sarcopenic-obese	1.42 (1.05 – 1.91)*	1.35 (0.99 – 1.82)	1.28 (0.94 – 1.74)
Stroke			
Normal	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Obese	1.04 (0.77 – 1.41)	1.03 (0.76 – 1.39)	1.10 (0.81 – 1.49)
Sarcopenic	1.09 (0.80 – 1.48)	1.06 (0.78 – 1.44)	0.88 (0.64 – 1.21)
Sarcopenic-obese	1.16 (0.80 – 1.67)	1.10 (0.76 – 1.59)	0.95 (0.65 – 1.37)

Results are reported as hazard ratio (95% confidence interval). * P<.05 versus referent group; Model 1: adjusted for age, sex, race, income, smoking, alcohol, and cognitive function; Model 2: same as Model 1 + physical activity; Model 3: same as Model 2 + cardiometabolic risk markers (diabetes, hypertension, HDL-cholesterol, total cholesterol, and triglycerides).

When based on measures of obesity X muscle strength, the risks of CVD, CHD, CHF, and stroke were not significantly elevated in either the obese or sarcopenic groups compared to the normal group after adjusting for the basic covariates with one exception (Model 1, Table 4). However, compared to the group with a normal body composition the risk of CHF was elevated by 42% (P=0.02) and the risk of CVD was increased by 23% (P=0.06) in the sarcopenic-obese group compared to the normal group. When physical activity was added in Model 2, the hazard ratios were attenuated in most cases. Additional adjustment for CVD risk factors (Model 3) further attenuated the hazard ratios, which were no longer statistically significant.

The risk estimates for overall CVD and its subtypes within the sarcopenic-obese group were not significantly different from those in either the sarcopenic or obese groups as evident by the overlapping confidence intervals for the hazard ratios (Tables 3 and 4).

Discussion

The impact of sarcopenic-obesity on physical function has been given considerable attention in the gerontology literature; however, the impact of this condition on cardiovascular health has been poorly studied. To our knowledge, this is the first prospective study to examine the relation between sarcopenic-obesity and CVD risk. The findings indicate that muscle strength is more important for CVD risk than muscle mass. Although obesity and sarcopenia alone did not significantly predict CVD, when they occurred simultaneously (e.g., sarcopenic-obesity) the risk of CVD increased by 23%. Furthermore, the present study indicates that the relation between sarcopenic-obesity and CVD is explained in part by the effects of physical activity and common CVD risk markers.

Previous research has defined sarcopenic-obesity using low height-adjusted skeletal muscle mass coupled with high percent body fat. Using these criteria, studies have identified an increased risk of physical disability and functional impairment in sarcopenic-obese persons (1, 2). For example, using a prospective cohort study design Baumgartner and colleagues (2) found that sarcopenic-obese elderly were 2.5 times more likely to have a decline in physical function compared to elderly with a normal body composition. Purely sarcopenic and obese persons were not at increased risk. In the present study, WC was used instead of percent body fat and when a high WC was coupled with low grip strength, the pattern observed for CVD risk in this study were similar to those reported by Baumgartner and colleagues for physical disability (2). However, the magnitude of effect for sarcopenic-obesity was considerably weaker in the present study compared to previous observations for physical function.

Our finding that sarcopenic-obesity was associated with a modestly increased risk of CVD and CHF was opposite to the results of Aubertin-Leheudre and colleagues (14). These authors reported that the cardiometabolic risk factor profile was, surprisingly, more favorable in sarcopenic-obese postmenopausal women than in obese postmenopausal women who were not sarcopenic. In that small cross-sectional study, the purely obese women had 41% more visceral fat than the sarcopenic-obese women, which may explain why the cardiovascular risk factors were different in these two groups. While the abdominal fat content was not well matched in the

two obese groups in that study, in the present study the purely obese and sarcopenic-obese groups had comparable waist circumference values, suggesting that their abdominal fat content was similar.

The conflicting results between our different definitions of sarcopenic-obesity imply that muscle quality (e.g., strength) is more important than muscle quantity (e.g., mass) in aging humans. While muscle strength and muscle mass are related, they are not one and the same as evidenced by the weak correlations between these measures. Previous work demonstrated that only leg strength was independently associated with lower extremity functional performance when leg strength and leg muscle were considered in the same regression model (27). Muscular strength also appears to be important for cardiometabolic health as evidenced by the present findings and those of Jurca and colleagues (11), who reported lower incidence of the metabolic syndrome across muscular strength tertiles in men. Together, these results suggest an important function for muscular strength that extends beyond the role of muscle mass.

Inclusion of physical activity and common CVD risk markers as covariates in the mediation regression models attenuated the risk estimates for the CVD outcomes in the sarcopenic-obese subjects. For example, the increased risk of CVD associated with sarcopenic-obesity based on muscle strength was attenuated from 23% to 18% after controlling for physical activity, and further reduced to 6% after controlling for CVD risk markers. This suggests that the pathway through which sarcopenic-obesity influences CVD outcomes, at least in part, involves physical activity and common CVD risk markers. That is, sarcopenic-obesity may lead to inactivity and an elevation in CVD risk markers, which in turn would increase the risk of CVD events. Previous research supports the protective role of muscle strength as increases in strength have been associated with improvements in high-density lipoprotein cholesterol (28), blood pressure (29), and insulin sensitivity (30); although a literature review in this area (31) indicated that the effects of muscle strengthening activities on CVD risk factors is inconsistent. Furthermore, there is an abundance of evidence indicating that abdominal obesity in the elderly negatively affects several CVD risk markers including hypertension, impaired glucose metabolism, and dyslipidemia (32).

A recent study demonstrated that abdominal obesity is associated with an upregulation of proinflammatory cytokine production (12). These cytokines in turn are inversely related to muscle strength, thereby providing a link by which obesity may lead to sarcopenic-obesity over time. However, due to the cross-sectional design of that study (12), the cause-and-effect nature of the relation between abdominal fat and muscle is uncertain. Other research has reported that these same proinflammatory cytokines are risk factors for CVD (33, 34). Therefore, although speculative at this time, abdominal obesity may represent the starting point of sarcopenic-obesity.

In light of the current findings, public health efforts should continue to promote regular physical activity and balanced nutrition to assist with maintenance of optimal body composition through adulthood and into old age. For elderly persons who are sarcopenic-obese, treatment would ideally focus on decreasing abdominal fat while simultaneously improving muscle strength.

There are limitations to the present study that warrant consideration. Although reasonably accurate for use in large studies, BIA and WC are not criterion measures of body composition. The imprecision of these measures may have weakened the relationship between sarcopenia and obesity with CVD risk. Furthermore, although related to more definitive measures of strength (19), hand grip strength is only a proxy of overall muscular strength.

In summary, sarcopenic-obesity, as determined by a high WC and low hand grip strength, was associated with a 23% increased risk of CVD in a large sample of community-dwelling elderly adults. This relationship was not apparent when body composition was classified using muscle mass, suggesting that strength may be more important than muscle mass for CVD prevention.

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References

1. Baumgartner RN. Body composition in healthy aging. Ann N Y Acad Sci 2000;904:437-448.
2. Baumgartner RN, Wayne SJ, Waters DL, Janssen I, Gallagher D, Morley JE. Sarcopenic obesity predicts instrumental activities of daily living disability in the elderly. Obes Res 2004;12:1995-2004.
3. Davison KK, Ford ES, Cogswell ME, Dietz WH. Percentage of body fat and body mass index are associated with mobility limitations in people aged 70 and older from NHANES III. J Am Geriatr Soc 2002;50:1802-1809.
4. Zoico E, Di Francesco V, Guralnik JM et al. Physical disability and muscular strength in relation to obesity and different body composition indexes in a sample of healthy elderly women. Int J Obes Relat Metab Disord 2004;28:234-241.
5. Despres JP, Lemieux S, Lamarche B et al. The insulin resistance-dyslipidemic syndrome: contribution of visceral obesity and therapeutic implications. Int J Obes Relat Metab Disord 1995;19 Suppl 1:S76-86.
6. Boyko EJ, Fujimoto WY, Leonetti DL, Newell-Morris L. Visceral adiposity and risk of type 2 diabetes: a prospective study among Japanese Americans. Diabetes Care 2000;23:465-471.
7. Despres JP, Moorjani S, Lupien PJ, Tremblay A, Nadeau A, Bouchard C. Regional distribution of body fat, plasma lipoproteins, and cardiovascular disease. Arteriosclerosis 1990;10:497-511.
8. Nicklas BJ, Penninx BW, Cesari M et al. Association of visceral adipose tissue with incident myocardial infarction in older men and women: the Health, Aging and Body Composition Study. Am J Epidemiol 2004;160:741-749.
9. Snijder MB, Henry RM, Visser M et al. Regional body composition as a determinant of arterial stiffness in the elderly: The Hoorn Study. J Hypertens 2004;22:2339-2347.
10. Snijder MB, Dekker JM, Visser M et al. Larger thigh and hip circumferences are associated with better glucose tolerance: the Hoorn study. Obes Res 2003;11:104-111.
11. Jurca R, Lamonte MJ, Barlow CE, Kampert JB, Church TS, Blair SN. Association of muscular strength with incidence of metabolic syndrome in men. Med Sci Sports Exerc 2005;37:1849-1855.
12. Schrager MA, Metter EJ, Simonsick E et al. Sarcopenic obesity and inflammation in

the InCHIANTI study. J Appl Physiol 2007;102:919-925.
13. Pearson TA, Mensah GA, Alexander RW et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation 2003;107:499-511.
14. Aubertin-Leheudre M, Lord C, Goulet ED, Khalil A, Dionne IJ. Effect of sarcopenia on cardiovascular disease risk factors in obese postmenopausal women. Obesity (Silver Spring) 2006;14:2277-2283.
15. Fried LP, Borhani NO, Enright P et al. The Cardiovascular Health Study: design and rationale. Ann Epidemiol 1991;1:263-276.
16. Janssen I, Heymsfield SB, Allison DB, Kotler DP, Ross R. Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous, and visceral fat. Am J Clin Nutr 2002;75:683-688.
17. Lukaski HC, Johnson PE, Bolonchuk WW, Lykken GI. Assessment of fat-free mass using bioelectrical impedance measurements of the human body. Am J Clin Nutr 1985;41:810-817.
18. Janssen I, Heymsfield SB, Baumgartner RN, Ross R. Estimation of skeletal muscle mass by bioelectrical impedance analysis. J Appl Physiol 2000;89:465-471.
19. Rantanen T, Era P, Kauppinen M, Heikkinen E. Maximal isometric muscle strength and socioeconomic status, health, and physical activity in 75-year-old persons. J Aging Phys Act 1994;2:206-220.
20. Tracy RP, Arnold AM, Ettinger W, Fried L, Meilahn E, Savage P. The relationship of fibrinogen and factors VII and VIII to incident cardiovascular disease and death in the elderly: results from the cardiovascular health study. Arterioscler Thromb Vasc Biol 1999;19:1776-1783.
21. Ives DG, Fitzpatrick AL, Bild DE et al. Surveillance and ascertainment of cardiovascular events. The Cardiovascular Health Study. Ann Epidemiol 1995;5:278-285.
22. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.
23. Siscovick DS, Fried L, Mittelmark M, Rutan G, Bild D, O'Leary DH. Exercise intensity and subclinical cardiovascular disease in the elderly. The Cardiovascular Health Study. Am J Epidemiol 1997;145:977-986.
24. American Diabetes Association. Screening for type 2 diabetes. Diabetes Care 2003;26:21-24.
25. Chobanian AV, Bakris GL, Black HR et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003;289:2560-2572.
26. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). Jama 2001;285:2486-2497.
27. Visser M, Newman AB, Nevitt MC et al. Reexamining the sarcopenia hypothesis. Muscle mass versus muscle strength. Health, Aging, and Body Composition Study Research Group. Ann N Y Acad Sci 2000;904:456-461.
28. Hurley BF, Hagberg JM, Goldberg AP et al. Resistive training can reduce coronary risk factors without altering VO2max or percent body fat. Med Sci Sports Exerc 1988;20:150-154.
29. Martel GF, Hurlbut DE, Lott ME et al. Strength training normalizes resting blood pressure in 65- to 73-year-old men and women with high normal blood pressure. J Am Geriatr Soc 1999;47:1215-1221.
30. Ryan AS, Hurlbut DE, Lott ME et al. Insulin action after resistive training in insulin resistant older men and women. J Am Geriatr Soc 2001;49:247-253.
31. Hurley BF, Roth SM. Strength training in the elderly: effects on risk factors for age-related diseases. Sports Med 2000;30:249-268.
32. Villareal DT, Apovian CM, Kushner RF, Klein S. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. Obes Res 2005;13:1849-1863.
33. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 2000;342:836-843.
34. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 1997;336:973-979.